Liver Transplantation in Hawaii: The initial five years

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Abstract

Twenty-one liver transplants have been performed in Hawaii in the initial five years. Hepatitis C was the most common reason for liver transplant . Twenty patients are currently alive, and 93.3% of patients survived one year. Of those one year post transplant, 60% have returned to work. Liver transplant can be performed in Hawaii with results comparable to mainland centers.

Methods and Materials

This is a retrospective review of patients who underwent liver transplant at St. Francis Medical Center from May 1993 to May 1998. Records were reviewed for demographic data, etiology of liver disease, status at the time of transplant, length of surgery, amount of blood transfused, length of intensive care unit (ICU) and hospital stay, complications and outcome. We also determined cold ischemic time (CIT), which is the length of time between aortic cross-clamp in the cadaveric donor and the time of revascularization of the liver in the recipient. Outcome was determined by patient and allograft survival, number of rejection episodes, recurrence of disease, need for retransplantation, and return to work.

We reviewed data on patients referred to our transplant center for liver transplant evaluation during this same time period. Reasons for not transplanting these patients at our center were noted.

We also reviewed demographic data on cadaveric donors for these transplant recipients. Aggregate data on donors during this 5-year period were also obtained from the Organ Donor Center of Hawaii, the official Organ Procurement Organization (OPO) for the state of Hawaii.

Results

Twenty-one liver transplants were performed at St. Francis Medical Center in the first five years since inception of the program in May 1993. There were 11 males and 10 females with a mean age of 52.0 years (range 39-62 years). In terms of race distribution, there were 7 Caucasians, 6 Japanese, 5 Filipinos, and one each for Chinese, Korean, and Hispanic-American extraction. Etiology of end-stage liver disease was predominantly Hepatitis C (13 of 21 patients). Other etiologies included alcoholic cirrhosis (3 patients), Hepatitis B (2 patients), autoimmune hepatitis (2 patients) and cryptogenic (1 patient). Two patients also had hepatocellular cancer at the time of transplant, in addition to their underlying disease. (Hepatitis B in one and Hepatitis C in the other).

Seventeen patients were waiting at home when called in for liver transplant. Four patients were in the hospital – 2 in the intensive care unit, and 2 on the general medical floor when a donor organ became available.

Mean operative time was 9.1 ± 2.3 hours (range 6-15.5 hours). Patients received a mean of 13.3 ± 18.0 units of packed red blood cells (PRBCs). The amount of blood transfused in the last 16 transplants was 6.2 ± 3.3 units. This may be multifactorial and may include the use of antifibrinolytic agents such as aprotonin given intravenously during these most recent 16 procedures. Mean ICU stay was 7.4 ± 11.4 days (range 1-49 days) with 11 patients remaining in the ICU for 3 days or less. Mean hospital stay was 18.0 ± 16.7 days (range 6-71 days) with 10 patients hospitalized for less than 10 days. (Hospital/ICU length of stay based on 20 patients, as one patient currently hospitalized)

Early complications which required return to the operating room within the first 30 days, included bleeding (2 patients) and bile leak requiring biliary reconstruction (2 patients). One patient also required return to the operating room after she accidentally removed her T-tube on post-operative day 4, and another patient required drainage of a mucocele of the cystic duct stump.

Infectious complications in the initial hospitalization included Vancomycin-resistant enterococcal peritonitis in one patient and fungal line sepsis in a second patient. Two patient developed opportunistic infections during the post-transplant period. One of these patients developed a Herpes simplex viral infection manifested by skin lesions, fever, and mouth/pharynx ulcerations. This resolved with use of acyclovir and lowering of immunosuppression. A second patient developed a respiratory symptoms and a lung mass with needle biopsy yielding Candida albicans. This mass resolved with a course of fluconazole.

Two patients suffered cerebrovascular accidents 1.5 and 28 months post-transplant. One of these patients also sustained a femoral neck fracture shortly after the cerebrovascular accident. Both patients have recovered well with no noticeable residual deficits.

Thirteen patients underwent transplant for Hepatitis C. Of these, seven have had liver biopsies for elevated liver enzymes. Five of these demonstrated histologic evidence of recurrence. Immunosuppression has been lowered in these patients. One patient has been placed on interferon for histologic progression of hepatitis C, with evidence of early fibrosis. There has been no graft loss due to recurrent hepatitis C. Two patients with hepatitis B, have been followed closely for recurrence of disease. Hepatitis B immune

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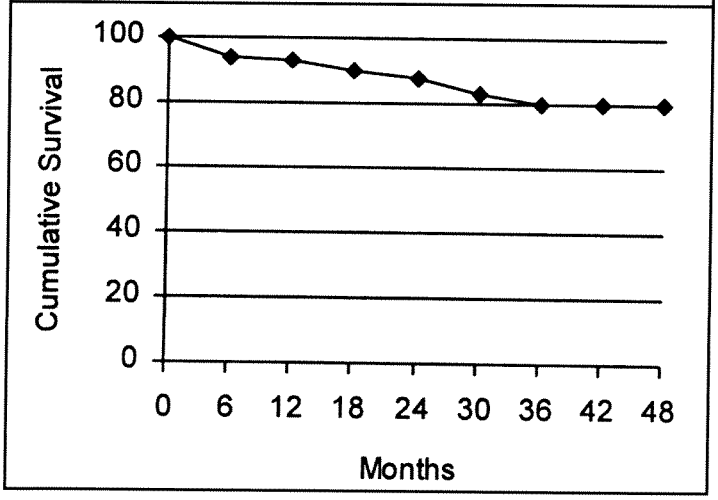
globulin has been administered prophylactically every 3-4 weeks to maintain a Hepatitis B surface antibody titer of greater than 300 mIU/ml. Patients have also been placed on lamivudine, a nucleoside analog which decreases the replication of the hepatitis B virus. Neither patient has demonstrated any evidence of recurrence of disease.

During this same time period, a total of 53 other patients were referred to our center for possible liver transplant evaluation. Six patients were evaluated and placed on the waiting list, but expired from complications of liver failure before a donor liver became available. Two patients were removed from the waiting list –one because the patient no longer desired transplant and the other due to alcohol recidivism after 2 years of abstinence. Ten patients were evaluated but decided to pursue transplant at mainland centers for various reasons. Twenty-three patients were not completely evaluated for either medical reasons (other severe underlying diseases, HIV positivity, or sepsis), psychosocial reasons (recent substance abuse, severe psychiatric problems) or financial reasons (insurance coverage contracted with mainland centers). Twelve patients did not pursue transplant evaluation any further despite physician referral and multiple attempts at contacting them.

Donor livers were obtained from the state of Hawaii only. No imported livers from the mainland were accepted during this time period. Mean donor age was 34.0 ± 15.2 years (range 12 to 55 years.) During this time period 41 livers were sent to mainland centers, because of inappropriate size or blood type for the potential recipients on our list. Several of these livers were of marginal quality (age >55 years, elevated liver tests, and/or high doses of vasopressors in the donor) and were not felt to be suitable at that time. Mean cold ischemia time was 388 ± 110 minutes (range 168-619 minutes).

Six patients experienced transplant rejection. Five of these patients improved with a high-dose intravenous steroid bolus (500-1000mg). The sixth patient required a course of OKT3 (monoclonal antibody). Of the 15 patients who are at least 1-year post transplant, 14 are alive and functioning well, for a one year survival of 93.3% (See figure 1). One patient died at 3 months from complications of portal vein thrombosis and sepsis. No patient has required retransplantation. Of these 15 patients, 9 (60%) are currently working at part-time or full-time jobs.

Figure 1: Kaplan-Meier Survival Curve for liver transplant patients 1993-1998.



Discussion

Five years ago our group published an article in this journal on Hawaii's first liver transplant. Since that time, the transplant program in Hawaii has continued to thrive and has demonstrated that liver transplants can be performed here with results comparable to other US transplant centers. Our 1 year patient/graft survival was 93.3% and nationwide, the 1 year patient and graft survival was 87.0% and 79.1%, respectively. One year survival by UNOS (United Network for Organ Sharing) status was 92.3%, 100%, and 50% for status 3, 2, and 1 respectively. This is compared to 84.0%, 77.1% and 67.1% for the national data.[1] (Status 1 patients are waiting in the ICU, see below)

Liver transplantation has become a standardized treatment for end-stage liver disease. Surgeons have refined the operative procedure, and many new immunosuppressive drugs have helped minimize rejection. Other new advances include successful use of Hepatitis B immune globulin and nucleoside analogs, such as lamivudine to prevent recurrence of Hepatitis B.[2] We have also begun to understand the appropriate use of liver transplant for malignancies. When done in patients with smaller size (<5 cm), and without lymphatic spread, vascular invasion, or multiple nodules, the prognosis is better. Adjuvant modalities such as chemoembolization, and percutaneous ethanol may be used to treat the tumor while waiting for the appropriate donor.[3] These modalities may also prevent recurrence of cancer, but it is difficult to know — they may only be delaying the recurrence. Longer follow-up studies will be necessary.

We still need to find the appropriate treatment for recurrent Hepatitis C. Whether interferon and use of new antiviral agents will help has not been completely determined.[2] Ultimately finding ways to treat Hepatitis C before progression to end-stage cirrhosis, will be the most beneficial.

The major problem facing all liver transplant programs, however, has been that of a limited supply of donor organs for the rapidly growing waiting list. Because of this, the transplant community continuously tries to improve the process of donor allocation and distribution in order to maximize use of this precious resource.

The indications for liver transplant continue to include irreversible advanced chronic liver disease, fulminant liver failure, metabolic liver diseases and certain neoplastic diseases. We continue to look for complications such as intractable ascites, variceal bleeding, encephalopathy, malnutrition, hepatorenal syndrome and recurrent spontaneous bacterial peritonitis as indications that a liver transplant will be needed soon. However, we are now unable to place a patient on the waiting list until specific criteria are met

Listing criteria is based on the Childs-Turcotte-Pugh score (CTP score, see table 1). Each patient is assigned a score based on albumin, bilirubin, prothrombin time, encephalopathy, and ascites. The score is used to give each patient a status.

Status1: Fulminant liver failure

Status2A: CTP score ≥10 in ICU and have at least 1 of the following:
acute variceal bleed, hepatorenal syndrome, refractory acites, stage III/IVencephalopathy

Patient cannot be listed as Status 2A if extrahepatic sepsis, high dose or 2 or more pressures, or irreversible multi-organ failure

Status 2B: CTP score ≥10 or CTP score ≥7 and 1 of the following: acute variceal bleed, hepatorenal syndrome, spontane ous bacterial peritonitis, refractory ascites

Status 3: Patient requires continuous medical care, with CTP score ≥7

Table 1: Summary of Data	
Number of Patients	21
Mean age	52.0 years
M:F	11:10
Etiology	
Hepatitis C	13 patients
Alcohol	3 patients
Hepatitis B	2 patients
Autoimmune	2 patients
Cryptogenic	2 patients
Mean operative time	9.1 ± 2.3 hours
Mean, blood transfusions	13.3 ± 18.0 units
Mean ICU stay	7.4 ± 11.4 days
Mean hospital stay	18.0 ± 16.7 days
#with rejection	6 patients
#currently employed	9 patients
1 year graft/patient survival	93.3%

Table 2: Childs-Turcotte-Pugh Score			
Points	**1**	**2**	**3**
Encephalopathy	None	Grade 1-2	Grade 3-4
Ascites	Absent	Slight (controlled with diuretics)	Moderate
Bilirubin (mg/dl)	<2	2-3	>3
Albumin (g/dl)	>3.5	2.8-3.5	<2.8
Prothrombin time (sec prolonged)	<4	4-6	>6
For primary biliary cirrhosis, other cholestatic liver diseases. Bilirubin (mg/dl)	<4	4-10	>10

United Network for Organ Sharing (UNOS) is an organization, which exchanges scientific information, compiles statistical data, promotes organ donation and creates policy for all organ allocation/ distribution. Members of UNOS include transplant centers, organ procurement organizations, transplant physicians, histocompatibility laboratories, and members of the community including transplant recipients and donor families.

UNOS has developed various policies for organ allocation depending on the type of organ transplanted. UNOS has divided the US into 11 different regions – Hawaii is a part of Region 5. Factors which are generally involved in organ allocation include blood type, size of the patient, waiting time, and medical urgency status.

When a donor liver becomes available, it is offered to the patient of compatible blood type and size and in the order of medical urgency (Status 1 first) locally, then within the region, then within the United States (US). If a liver becomes available in Hawaii, it is offered to local patients first. If no suitable patient is found then it will be offered to the centers within Region 5. If no one in region 5 accepts the organ, it may be used anywhere in the US.

UNOS has developed the standardized listing criteria outlined above in order to avoid listing patients too early or transplanting patients with unreasonable likelihood for survival. It allows for some uniformity in listing practices between the 121 liver transplant centers in the US.

The most controversial issue currently facing the transplant community is the intervention of the Department of Health and Human Services (HHS) on the practices of UNOS. Several of their principles include; "Transplant patients are best served by an organ allocation system that functions equitably on a nationwide basis" and "Organs should be equitably allocated to all patients, giving priority to those patients in most urgent medical need of transplantation, in accordance with sound medical judgment", Also, "The Secretary of HHS should represent the public interest by setting broad goals for the OPTN (Organ Procurement and Transplantation Network) and by overseeing OPTN policy development and operations with a view toward ensuring that the goals are being addressed in a reasonable manner".[5] While transplanting the sickest patients seems to make sense to the average person, studies have demonstrated that the sickest patients have the poorest survival and the highest hospital charges.[1,4,5] Furthermore, if there is a single national list of patients, donor organs may end up traveling longer distances to the sickest patients—thus prolonging the cold ischemic time and threatening graft function.

How any new rules will affect Hawaii is not clear at this time. Our program has had difficulty transplanting the sickest patients –with six patients dying while waiting on the list. Furthermore, only 9.5% of all patients transplanted were waiting in the ICU(status 1 or 2A) compared to the national average of 16%.[1] This may be due in part, to geographic isolation and difficulty sharing organs with mainland centers. The basic problem underlying the entire controversy or organ distribution, however, is the lack of enough donor organs to meet the ever-burgeoning list of patients waiting for transplant. Physicians and all health care professionals, should do their part for the organ shortage by promoting organ donation and promptly referring any potential donor.

References:

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